



General Toxicology Note



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VISIT...

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General Toxicology

- 1) Classification of Poisons?
- 2) Factors affecting action?
- 3) Fate.
- 4) Diagnosis.
- 5) Treatment.

Classification

- Origin (Source)
- Onset (Mode of exposure)
- Organ
- One Site or > 1 site (Site of action)

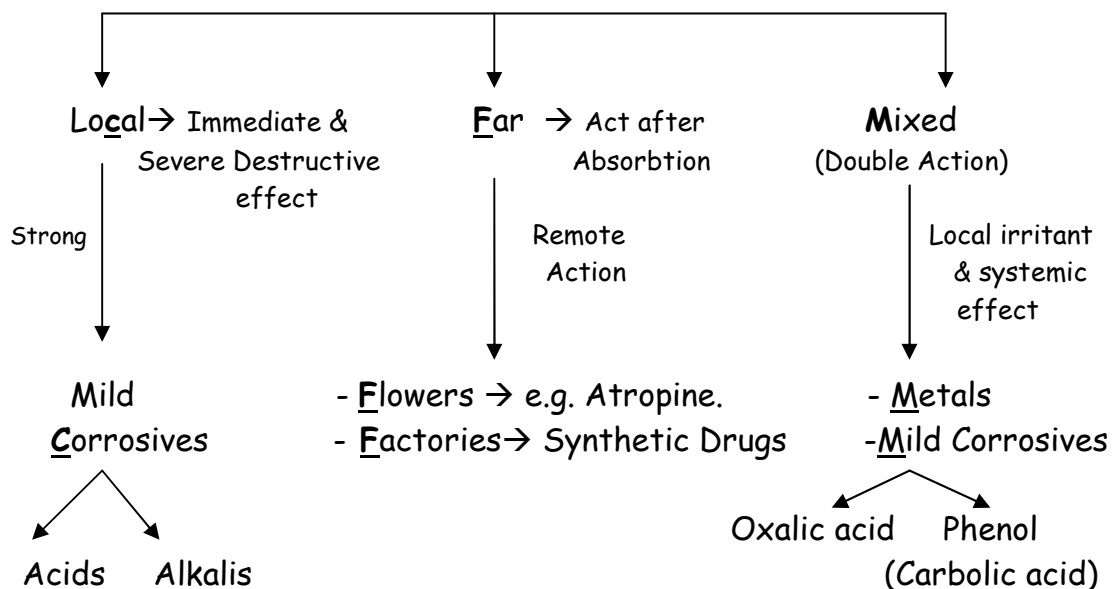
Origin & Source:

1. <u>Plants</u>	2. <u>Minerals</u> (<u>Metals</u>)	3. <u>Animal</u>	4. <u>Synthetic</u>
1. Opium ↓ Morphine ↓ Heroine 2. Atropine 3. Strychnine 4. Digitalis	-Lead -Mercury - <u>A</u> rsenic - <u>A</u> ntimony -Ph -Fe	- <u>S</u> nake. - <u>S</u> corpion. - <u>S</u> ea ↓ Marine animal's venom	<u>A</u> → <u>A</u> nalgesics <u>B</u> → <u>B</u> arbiturates (Hypnotics) <u>C</u> → <u>C</u> yclic Antidepressant (Psychotropics)

Organ Specificity:

- 1- Arsenic → Liver (Hepatotoxic).
 , Paracetamol
- 2- Digitalis → Heart
- 3- Aconite → Heart. } Cardiotoxic.
 خانق الذئب
- 4- Mercury → Micturation (Nephrotoxic).
 , Phenol (Kidney)
- 5- Neuro Toxins → Convulsants & Depressants.
- 6- Ocular Toxins → Methanol & Nicotine.
- 7- Dermal Toxins → Corrosives & AS & Hg.
- 8- Respiratory Toxins → Kerosene & Fumes.

Site of Action:



Mode of Exposure:

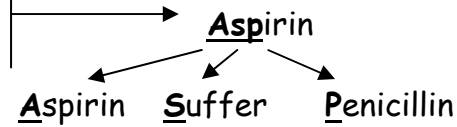
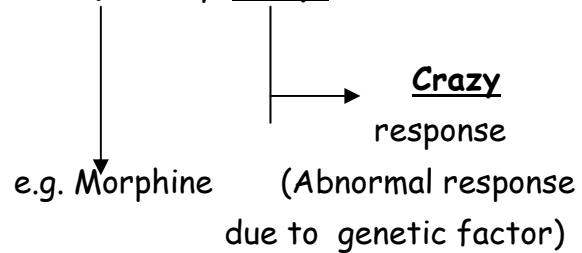
- 1- Acute → Single High Dose of the Poison.
- 2- Chronic → Repeated Small Dose of the Poison.

Factors affecting action of the poison

<u>Poison</u>	<u>Patient</u> 3S 5 Pharma
1- <u>Quantity</u> (Dose) 2- <u>Quality</u> (Form). 3- <u>Quickest</u> (Route Of Administration) } <u>3Qs</u> 1- <u>Quantity (Dose)</u> → X Severity → Vomiting → less effect. → Fatal Dose → Smallest amount → Death 2- <u>Quality (Form)</u> → Gas > Liquid > Solid - Powders > Lumps → Solubility → Concentration 3- <u>Quickest route</u> (route of administration) IV > Inh. > IM > s.c (skin) > through mucous membrane > intradermal (skin).	"3S" 1- <u>S</u>mall Or Old (Age) Children can tolerate Atropine. 2- <u>S</u>trong Or Not (Healthy) Liver Kidney } ↓ Detoxification & Excretion ↑ Toxicity 3- <u>S</u>tomach (MCQ) → Empty Or <u>F</u>ull. السوائل (خير) ↓ Rapid Absorption الأكل (شر) ↓ Rapid Absorption Fatty Meals ↓ Rapid Absorption e.g. Achlorohydia ↓ e.g.: KCN → HCN Non Toxic Toxic ↓ Toxicity Of KCN ♀ Ph -As ♀ Mercury -Alcohol

"5 pharma"1) Allergy

- small non-toxic
- abnormal exaggerated response

2) Idiosyncrasy

3) Tolerance → (in addicts)

- ↓ Toxicity
- ↑ Dose → Produce same effect

4) Interaction

- i) Synergism → كاس و القرص
Barbiturates + Ethanol
- ii) Antagonism → المصري والمستورد
Ethanol + methanol

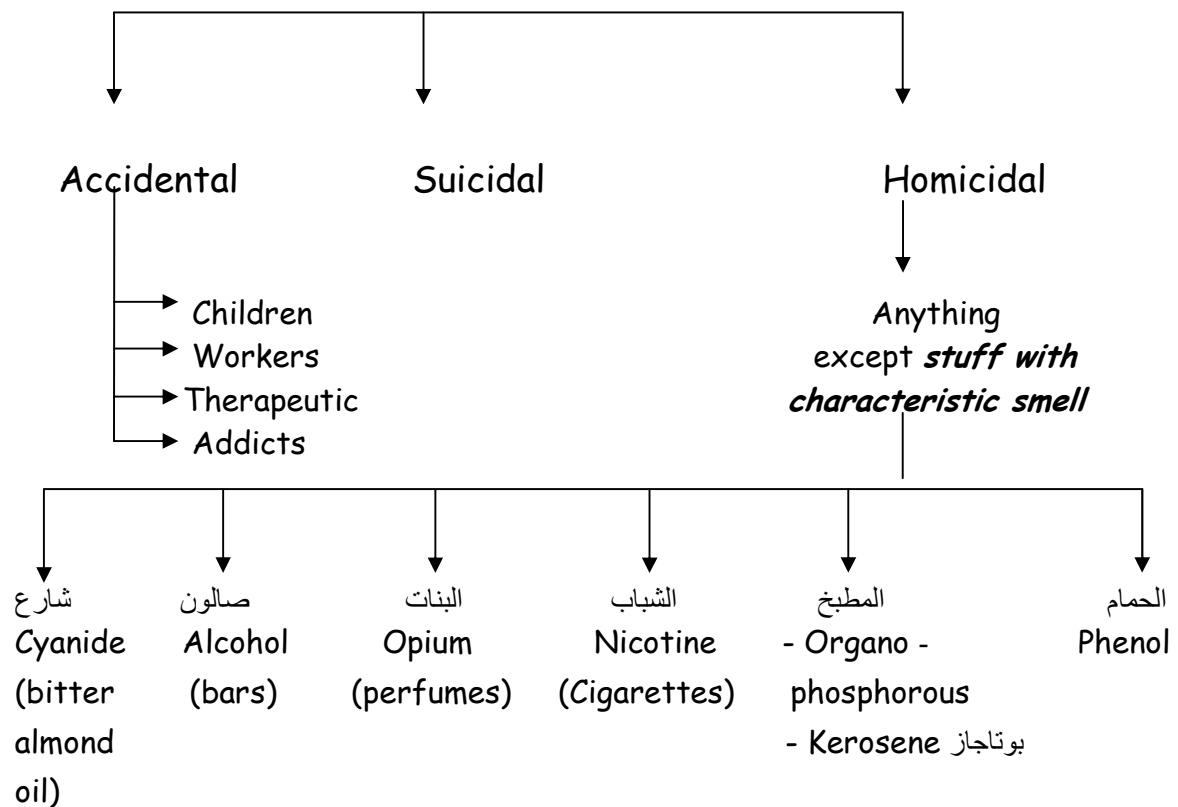
5) Cumulation

- E.g. → Digitalis
- Lead

Absorption	Distribution	Metabolism	Excretion
1- <u>Ingested</u> a) GIT → Stomach → Circulation b) Vomiting c) Stool		• <u>Liver</u> 	(1) <u>Kidney:</u> (2) <u>GIT:</u> (3) <u>Bile to Duodenum:</u>
2- <u>Inhaled</u> → Lung → Circulation			
3- <u>Injected</u> 			

Scheme

1. Condition of poisoning



2. Fatal dose

3. Fatal period

4. Action

5. Clinical picture

6. Ttt

7. Post-mortum picture

± 8. Source [classification]

± 9. Kinetics [ADME]

10. Diagnosis (Investigation)

Talk about

- (1) Circumstantial evidence
- (2) C/P
- (3) PM picture
- (4) Investigations (living and dead)

11. D.D.

Investigations

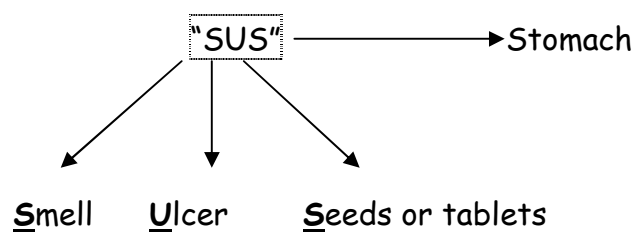
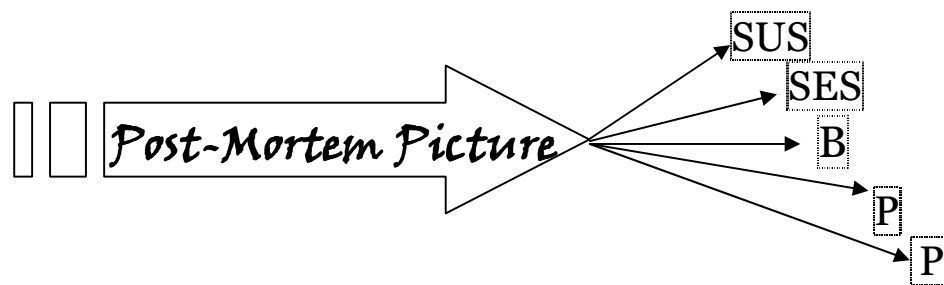
Living الخوارج	Dead التقطيع
(1) Blood	(1) Stomach
(2) Urine	(2) Intestine
(3) stool	(3) Blood
(4) Vomitus	(4) Kidney
(+) (5) Hair/nail	(5) Liver
	(6) Brain
	(7) H / N / B / T Metals في ال

General toxicology

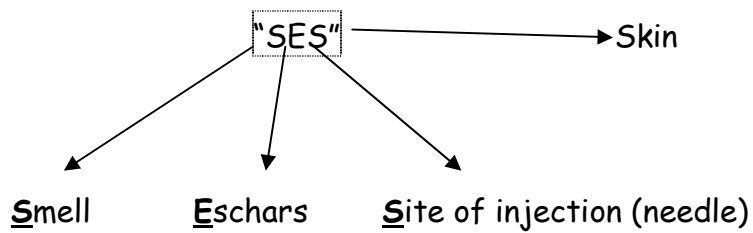
Action	Clinical picture
1) GIT	• Nausea • Vomiting • Colic • Diarrhea
2) Heart	• ↓ Pulse • ↓ Blood pressure } Arrest
3) Sensory nerve ↑ then ↓	• Tingling • Numbness • Hypersensation • Hyperthesia } then Anaesthesia
4) Motor nerve(N-M junction) ↑ then ↓	• Twitches • Tremors • Fasciculations • Convulsions } then Paralysis
5) CNS ↑	C H A I R Restlessness Irritability Anxiety Hypertension Convulsions
6) CNS ↓	"3Cs" • <u>C</u>oma • <u>C</u>yanosis • <u>C</u>entral asphyxia

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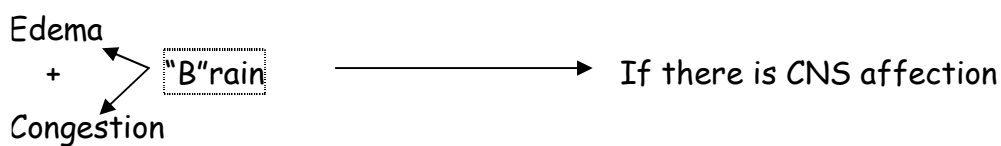
7) Renal failure	Oliguria + <u>A</u> <u>B</u> <u>C</u> then ↘ Anuria <pre> graph TD Oliguria --> A[Albumin] Oliguria --> B[Blood] Oliguria --> C[Cast] A --> Anuria B --> Anuria C --> Anuria </pre> <u>A</u>lbumin <u>B</u>lood <u>C</u>asts
8) Hepatic failure	1- Pain + tenderness in Rt hypochondrium. 2- Jaundice + Bleeding 3- ↑ Bilirubin + ↑ SGOT + ↑ SGPT 4- ↓ Albumin + ↑ Prothrombin time



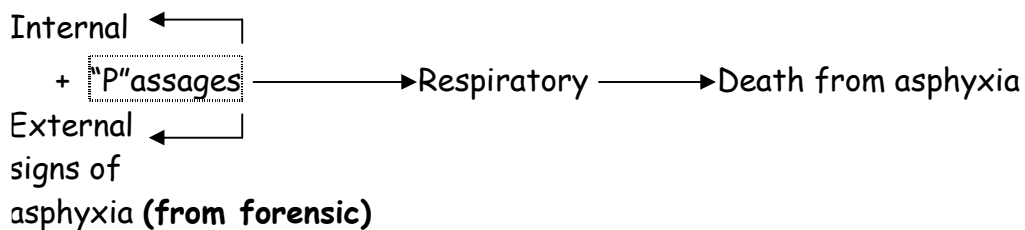
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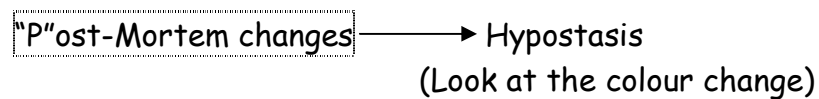
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Treatment:

- 1- Prevention of further exposure.
- 2- Supportive or symptomatic treatment.
- 3- Elimination of poison from GIT.
- 4- Destruction of poison in GIT & absorption (local antidotes).
- 5- Excretion of the absorbed poison.
- 6- Counteraction of the absorbed poison (physiological antidote).

Treatment

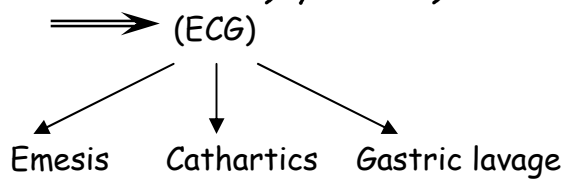
1- Prevention of further exposure:

- Factory (Industrial exposure)
 - Masks, gloves
 - Periodic-Medical Examination
 - Removal of patients
- Clinic → i.e. Hospitalization
 - Addicts
 - Suicidal & Homicidal
- House → Accidental poisoning among children

2- Supportive & Symptomatic treatment:

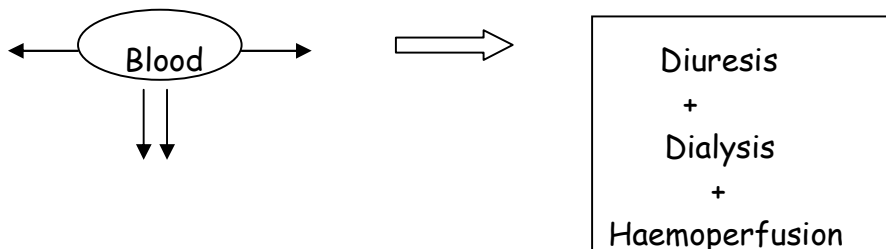
- Respiratory depression.
- CVS.
- Coma.

3- Elimination of poison from GIT:

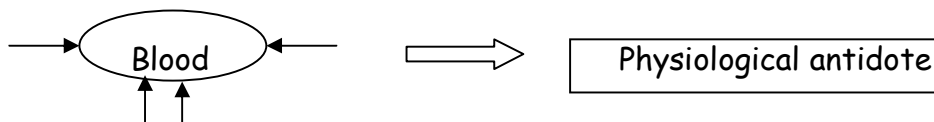


4- Destruction of poison in GIT & absorption: (Local antidotes)

5- Excretion of the absorbed poison:



6- Counteraction of the absorbed poison:

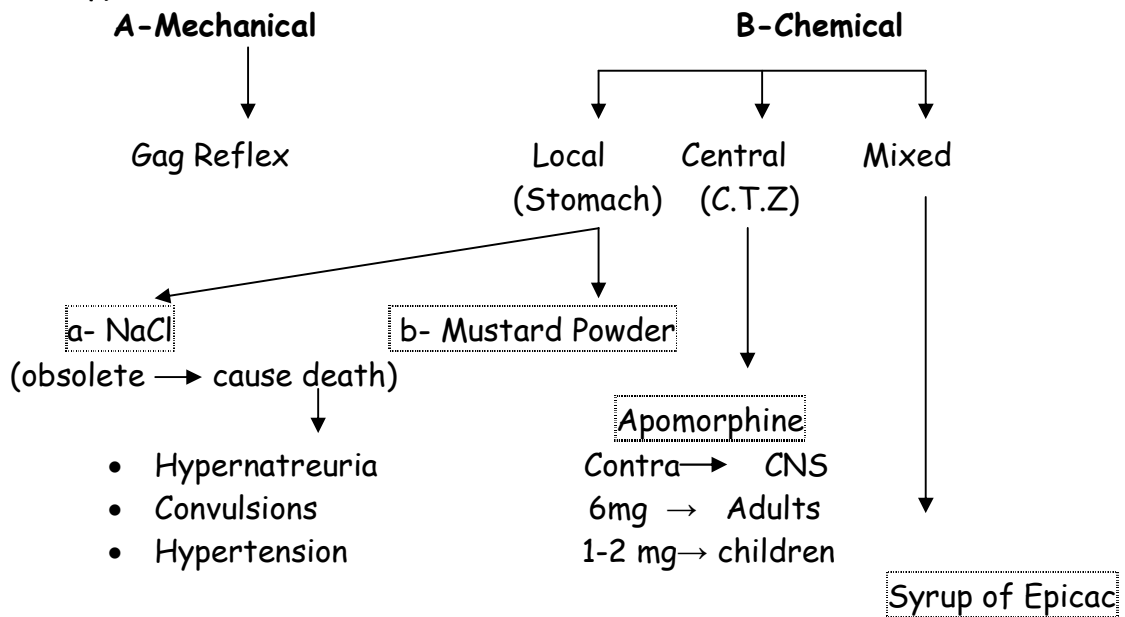


3- Elimination of poison from GIT: (ECG)

1) Emetics:

a- Def: Vomiting (3hrs)

b- Types:



1-Source: Plant (safe)

2-A.P: Emetine + Cephaline

3-Dose: 30ml/30 min

15ml/30min for children

4-Action

3- Contraindications:

Poisons	Patients
1- <u>C</u>orrosives & <u>K</u>erosene ↓ fear of perforation fear of chemical pneumonitis ↓ Stomach Esophagus Where vomitus is going back through the esophagus to the mouth. Because it is volatile	1- <u>C</u>omatosed → <u>A</u>sphyxia ↓ <u>A</u>spiration pneumonia 2- <u>C</u>onvulsions: Vomiting can stimulate convulsions. 3- <u>C</u>ardiac. 4- <u>G</u>IT → Esophageal varices Recent gastric operation 5- ↓ Cough reflex → e.g. old 6- Pregnant. 7- Elderly patients.

2- Cathartics: "Purgatives"

a- Action: Faster passage of poison through GIT → ↓ absorption

b- Types

زيت
Castor oil

↓

Avoid in fat soluble poison

ملح (Osmotic)

$MgSO_4$ (30 g in 300 ml H_2O & 250 mg/kg)
(Osmotic Purgative)
10% solution in children

3- Gastric lavage:

a- Def. → Evacuation / Washing / Tube

b- Indication → 3 hrs post-ingestion & emesis failed

Exception: can be done after 12 hrs in:

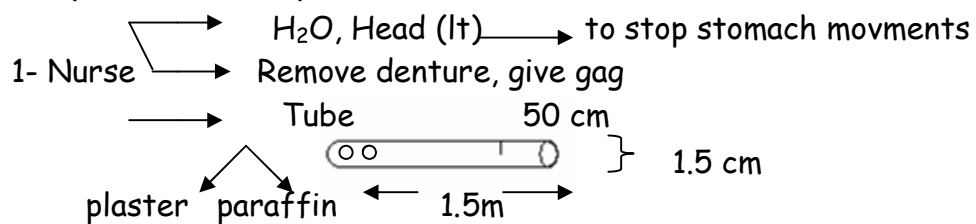
- 1) Secreted → e.g. Morphine+Antimony
- 2) Slow → Barbiturate
- 3) Sticky → Aspirin

Most effective

Easily absorbed drugs

- Hysterical
- Comatosed
- Uncooperative

c- Procedure (Refere to book)



2- Patient → Swallow

3- Doctor → Introduction

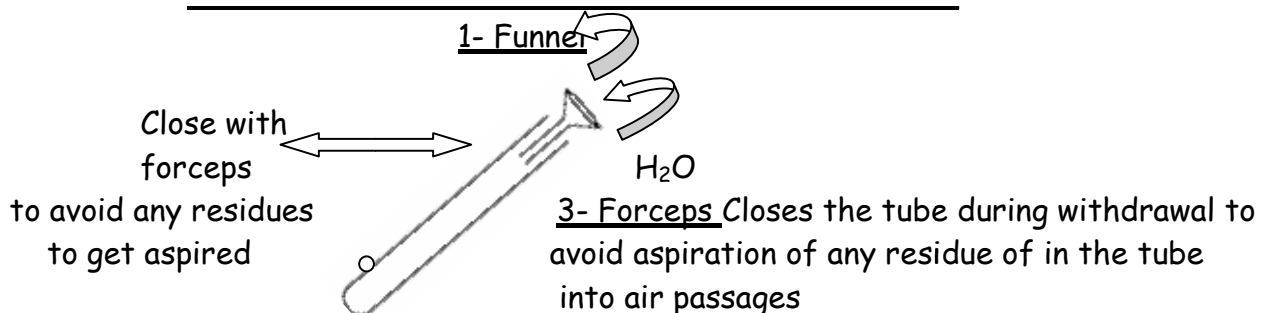
Ensure

Patient

- 1- Cough
- 2- Dyspnea
- 3- Cyanosed

Doctor

- 1- Ear
- 2- Hands
- 3- Eye



d- Contraindication:

I- Absolute CI: 1- Corrosives → Perforation by tube because → friable tissue

II- Relative CI :

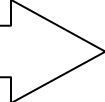
2- Kerosene (volatile) } insert cuffed endotracheal tube
3- Coma → due to fear from aspiration pneumonia
4- Convulsions → Inhalation anesthesia (Ether) →
to avoid ↑ freq. & severity of convulsions

e- Complications (Hazards):

- 1- Oesophagus → Perforation & bleeding
- 2- Trachea → Asphyxia
- 3- Lung → Aspiration pneumonia
- 4- Heart → Cardiac arrest
- 5- Psychic trauma
- 6- Gaging

3- Destruction of the poison in GIT:

Local antidotes



A - PHISCO-MECHANICAL:

2D 2C

1-Demulcent e.g. olive oil -egg white -milk → corrosives

2-Dissolvents e.g. 10% alcohol or glycerine → phenol
(followed by rapid gastric lavage)

3- Cotton

4-Charcoal (adsorbent)

a-origin : plant

b-uses: plants

metal

enterohepatic

*rew: bile to duodenum

c-dose: 50 gm / 500 ml H₂O every 4 hrs

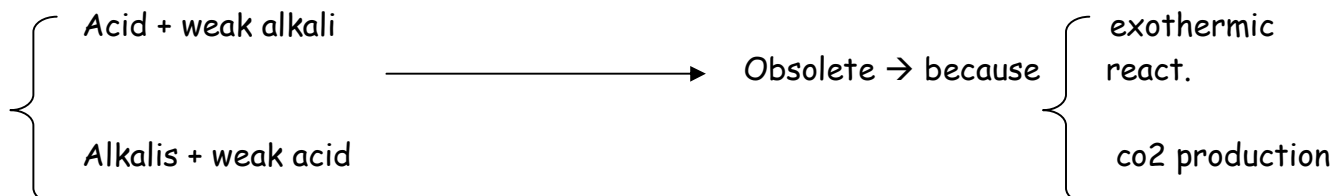
d-precautions: do not give it before syrup of epicac → it will be adsorbed

e- action: absorb the poison and it is not absorbed → raw charcoal

B-CHEMICAL:

By Chemical Reaction

1- Neutralization



2- oxidation H_2O_2 or $KMNO_4$

- Plants ← O_2 حبيب
 -Organophosphorus ← O_2 عدو
 -Cyanide ← عدو راسبوتين

3- precipitations شاي ثقيل

a) Tannic acid الفلاح

- 1) Plants (الغيط)
- 2) Antimony (المستوصف)

b) $Fe(OH)_3$ التفاحه → Arsenic (Napolion)c) $MgSO_4$ → Carbolic acid4) Reductiona) Ferric $\xrightarrow[\text{Citrus fruit after meal}]{\text{vitamin C}}$ ferrousb) Mercuric $\xrightarrow[\text{sulfoxylate}]{\text{Na formaldehyde}}$ mercurous .4- ELIMINATION OF POISON:

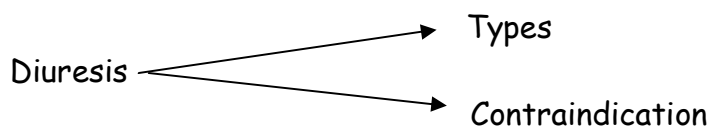
1 - LIVER → Detoxification (Biotransformation)

2- LUNGS → Resp. stimulant

3- GIT → Purgative

4- KIDNEY → Diuresis

5- BLOOD → Blood

KIDNEYTypes

1) Saline Diuresis ملح Na thio-sulphate ↓ معادن Heavy Metal Poisoning	2) Osmotic Diuresis ↓ Mannitol ↓ 10% ↓ 10gm ↓ IV infusion	3) Forced Diuresis				
		1) Principle	2) Types	3) Substance	4) Poison	5) Precautions
		Change PH of urine ↓ Ionization ↓ ↓ Absorption ↓ ↑ Excretion (Ion trap Phenomena)	1) Alkaline (PH > 7)	* NaHCO ₃ * Na lactate	Acid * Salicylic acid * Babbituric Acid	Fluid balance & electrolyte balance should be monitored
			2) Acid (PH > 5)	* NH ₄ Cl * Vit C (Ascorbic Acid)	* Amphetamine * Quinine	

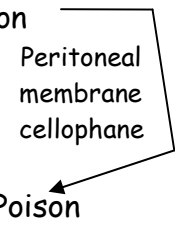
Contraindications of renal diuresis:-

- 1) Poison طريق
→ Not renal
- 2) Renal failure طريق مكسر
- 3) H₂O → Shock
- 4) K → Heart Failur

BLOOD

- a) Dialysis
- b) Haemoperfusion
- c) Plasma phoresis
- d) Exchange blood transfusion
- e) Chelators

1-Dialysis

*Indication	A) Peritoneal	B) Haemo (Artificial Kidney)
1) x x Diuresis 2) Renal failure 3) Coma	<u>*Procedure</u> 1) Evaluate bladder 2) Catheter → dialysate fluid similar to plasma è dextrose, heparine è procaine 3) 2 L after 1h 4) Syphonage ←	<u>*Procedure</u> Blood + poison  Blood - Poison <u>*Disadvantages:</u>
<u>*Precaution</u> Dialysable drugs only!!	<u>*Uses</u> الكحوليات Methanol & Ethylene glycol	<u>4 HIGH</u> " Ineffective" → 1) <u>High</u> ptn blood → 2) <u>High</u> Vol of Distribution → 3) <u>High</u> Lipid Bulk, passes the tissues → 4) <u>High</u> Molecular weight

1) Dialysis:

- Haemoperfusion → passage of anticoagulated blood via charcoal or resin columns .

- 1) Indication
- severe intoxication
 - high → barbiturates
 - hypothermia , hypotension , etc → coma

- 2) Procedure → adsorbs the poison

3) Effective for: removal of lipid soluble & ptn bound poisons e.g. barbiturates , salicylates & meprobamates .

- Exchange bl. Transfusion → 1) xxx dialysis
→ 2) ↓ VD → highly conc. In blood
- Plasma pheresis → removal of the plasma (vol. of distribution from the blood replace it with another sub)

2) chelators :

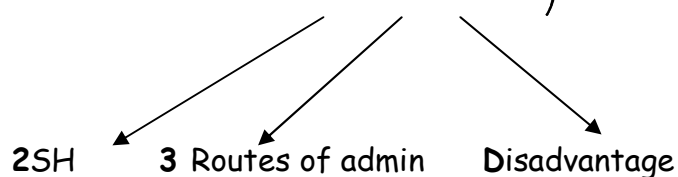
-Def. → + metals → non - toxic comp. → soluble & ↓ urine

- Types :
- (5) {
- 1) BAL
 - 2) DMSA
 - 3) EDTA
 - 4) Penicillamine
 - 5) Desferol

1) BAL → Anti - lewisite

↓
British

= (2 - 3 Dimercaprol)



→ Uses :

Lead
Arsenic
Gold

Mercury
Antimony
Bismuth

NMT 11

→ 2SH

→ 2 Analogues (DMSA & DMPS)

→ Routes of admin.: IM, eye drops & skin ointment
NEVER IV →→ embolism

→ Dose: 2.5 mg / kg → 2.5mg/kg/6 2 → Hr → days
2.5mg/kg/12 7 → then → days

Disadvantages of BAL :

- 1) plumbism (pb) : limited value in ttt as it chelates only lead in blood but not in bone & tissues .
- 2) pyrexia (anti-histaminics) → antihistaminics given to avoid allergic reaction .
- 3) bean (G-6-PD ↓↓↓) → haemolysis
- 4) BAL- Fe complex (iron) → more toxic than Fe

N.B. Answer for BAL + DMSA

2-DMSA Dimercapto-succinic acid (succimer)

Less toxic analogue
Of BAL

10mg /kg/ 8 5
Hr day

10 mg/ kg/ $\frac{12}{\text{Hr}}$ $\frac{2}{\text{weeks}}$

- a) Plumbism : from bone, blood&tissues
- b) Less toxic analogue of BAL
- c) G-6-PD DEF. : NO HAEMOLYSIS
- d) Fe

Better than BAL

e) Orally : without chelating with essential minerals (Ca, Mg , Fe, Cu, Zn)

f) Lead : ALAD enz. (A- aminolevulinic acid dehydrogenase) ← EDTA like

3- D-penicillamine (cuprimine) :

→ source : penicillin

→ Dose : 1 capsule/6h/10 days (as Antib)

- copper & zinc toxicity
- chronic toxicity of lead & mercury
- Contain 1 SH group (mono-thiol)

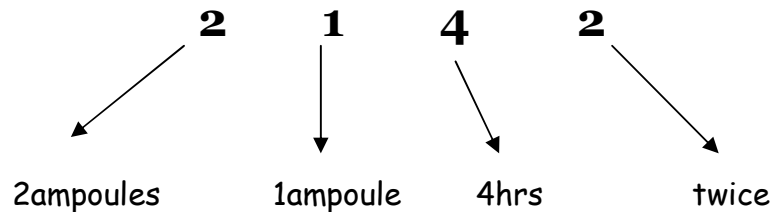
4- Desferol : (or desferoxamine)

- Fe toxicity
- Acts on iron in storage areas (ferritin & haemosidrin)

Dose

des fer ol

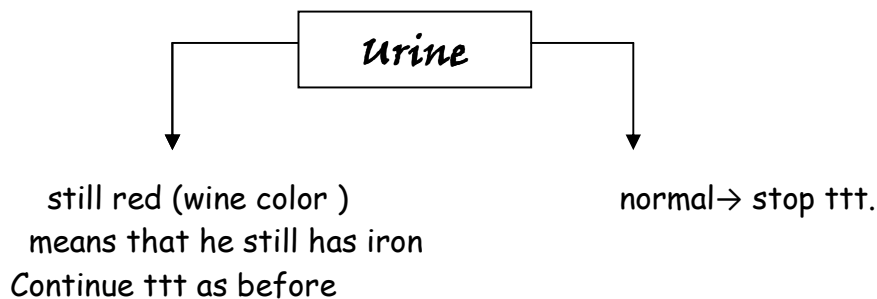
↓
دسته
↓
4hr



فریق کوره

1st : 2 ampoules

2nd : 1 ampoule every 4 hrs 2 times



BUT don not exceed 12 ampoules / day = 6 gm / day

Urine : normal → stop ttt

5- EDTA: (Ethyamine – diamine tetraacetic acid)

يحب اللبن → Ca

يحب الماء أكثر (ينزل في مواسير) → Lead

يذوب في السكر → Glucose

Dose:
1gm
Twice / day
5 days

Stop ttt 2 days then continue (to give chance for pb)

Types 3

- 1) di-sodium EDTA (has Ca) → lead toxicity
- 2) di-sodium EDTA (non- Ca) → digitalis toxicity
- 3) di-cobalt EDTA (kilocyanor) → cyanide toxicity

1- Di-sodium EDTA (with Ca)

+ Ca to spare body calcium, prevent chelation of Ca, prevent hypocalcaemia & tetany.

-If you Chelate any metal that has greater affinity for EDTa than Ca

e.g this is the case for lead which can replace Ca in complex forming poorly dissociable chelate that is rapidly excreted in urine.

2- Di-sodium EDTA (Non – Ca)

Given in digitalis toxicity because ppl with digitalis toxicity has hypercalcaemia

3- Di-sodium EDTA:

In cyanide toxicity

5- Counteraction of the absorbed poison:

*** physiological / systemic antidote

- 1) Chemical inactivator
- 2) Antagonistic antidote
- 3) Competitive antidote
- 4) Chelators (as before) + include it in answer

1) Chemical inactivators

e.g. N C B12

Na → Na thiosulfate → for metals → non toxic compounds

Ca → oxalic acid → inactivation

Ba → Hydroxycobalamine + cyanide toxicity → vit B12 (cyanocobalamine)

2) Antagonistic antidote:

Antagonise the pharmacological action of physiological mechanism .

e.g.

Atropine → Organophosphorus

Mephenisine → Strychnine
(Muscle relaxant)

3) Competitive antidote: antidote → compete with the poison for the receptor or compete with the receptor for poison

Examples : 3 M

a) **Morphine**: compete with the poison for receptors :

e.g. naloxone , nalorphine , levalorphine

Compete with Morphine on the opiate receptor

b) **Metals** : compete with the receptor for the poison

e.g. BAL & Resp. enz. compete for the Metals

c) **Mobeedat (organophosphorus)** : oximes compete with the receptor →
choline esterase enz. For the organophosphorus → preventing its binding to the enz..

Supportive & symptomatic ttt:

*** Supportive ttt:**

- 1) Respiratory depression
- 2) CVS → shock or collapse
- 3) CNS → coma
- 4) Acute hepatic failure
- 5) Kidney failure

1) Respiratory depression: 3A

Air passages

- Suction tube (remove secretions , vomitus, FB)
- Endotracheal tube
- Tracheostomy tube (in laryngeal obstruction & edema of Epiglottis)

Air → Carbogen

- maintain respiration
- 95% O₂- 5% CO₂ (stim. Respiration)

Artificial respiration

2) CVS → SHOCK OR COLLAPSE

1) elevate the leg with head downwards

2) vital signs affection :

* Respiratory → ↓ → give O₂

* Temp. → ↓ → ttt by warming

* B.P. → ↓ → dopamine / dobutamine → ↑ BP
→ plasma expanders e.g. glucose , manitol , ...etc .

* Pulse → Digitalis
→ Defibrillator
→ Anti-arrythmic drugs

3) CNS → Comatozed

2C { a) Change the posture (avoid bed sores & avoid pneumonia)
b) Catheterization (prevents urine retention & calculate amount of fluid coming out to balance fluid level)

c) Take care with respiratory affection (as before)

d) Care of cardiovascular (as before)

4-Kidney → Dialysis & Haemoperfusion failure

*R.F. Due to :-

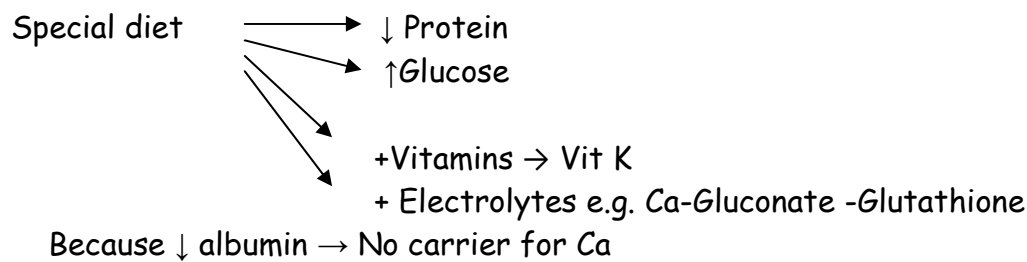
Direct Cause of R.F	Indirect Cause of R.F
1-Mercury → Mictureiton	↓Blood → Shock
2-Phosphorus	↓H ₂ O dehydration or electrolyte imbalance

5-Liver Failure:-

Causes → a) Arsenic (Napolion)
b) Paracetamol

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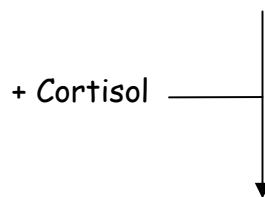
ttt:



*Symptomatic ttt:-

- 1) Cerebral Edema
- 2) Convulsions
- 3) Pulmonary Edema

1-Cerebral Edema → Osmotic Diuresis (By mannitol)



(Add it to any symptomatic ttt of edema)

2-Pulmonary edema →

Osmotic Diuresis

(Mannitol)+ Cortisone

+ Suction → Open passages by bronchodil.

+ O₂ under pressure

3-Convulsions:-

Strychnine → Most common Cause

ttt of convulsions → ttt of Strychnine

NMT11

